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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,736	08/11/2005	Mara Brancaccio	4636-25	7505

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EXAMINER	
HAMA, JOANNE	

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,736	BRANCACCIO ET AL.	
	Examiner	Art Unit	
	JOANNE HAMA	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8-15,17-20 and 23-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8-15,17-20 and 23-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant filed a response to the Non-Final Action of January 7, 2008 on April 7, 2008. Claims 2-7, 16, 21, 22, 26-42 are cancelled. Claims 1, 8-15, 17-20, 23-25 are amended.

Claims 1, 8-15, 17-20, 23-25 are under consideration.

It is noted that the Examiner has called Mr. Gary Tanigawa on July 1, 2008, to propose claim amendments to put the case into condition for allowance. Mr. Tanigawa returned the call on July 3, 2008, but could not guarantee that a response from Applicant regarding the claim amendments could be made before the instant Office Action was due.

Withdrawn Rejections

35 USC § 112, 2nd parag.

Applicant's arguments, see pages 6-7, filed April 7, 2008, with respect to the rejection of claims 8, 10, 11 have been fully considered and are persuasive. Applicant indicates that these claims have been amended. The rejection of claims 8, 10, 11 has been withdrawn.

35 USC § 103

Applicant's arguments, see pages 7-9 of Applicant's response, filed April 7, 2008, with respect to the rejection of claims 1-6, 15, 16, 20-22, 24, 25 as being unpatentable over Brancaccio et al. 1000 in view of Flatschart and Sogayar, 1999, and Capecchi, 1989 have been fully considered and are persuasive. Applicant has amended the

claims such that the claimed mice exhibit a phenotype. The rejection of claims of 1, 15, 20, 24, 25 has been withdrawn. It is noted that the rejection of claims 2-6, 16, 21, 22 is withdrawn as the claims are cancelled.

Applicant's arguments, see pages 7-9 of Applicant's response, filed April 7, 2008, with respect to the rejection of claims 1-4, 15, 20 have been fully considered and are persuasive. Applicant has amended the claims such that the claimed mice exhibit a phenotype. The rejection of claims 1, 15, 20 has been withdrawn. It is noted that the rejection of claims 2-4 is withdrawn as the claims are cancelled.

New/Maintained Objection/Rejections

Claim Objections

Claims 1, 8-15, 17-20 are newly objected to because of the following informalities. Claim 1, line 1, uses the phrase, "comprising disruption." The word, "a" appears to be missing between "comprising disruption". Appropriate correction is required. Claims 8-15, 17-20 depend on claim 1 and are included in the objection.

Claim 23, step ii) reads "a compound a compound." It appears that one of "a compound" is redundant.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 8-15, 17-20, 23-25 remain rejected in modified form under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

1) a transgenic mouse comprising a disruption in its endogenous melusin gene, wherein said mouse lacks expression of endogenous melusin, and wherein said mouse, after being subjected to a hypertensive condition, develops at least a phenotype selected from the group consisting of impaired heart hypertrophy, heart dilation, and heart failure,

2) a method of producing a transgenic mouse comprising a disruption in its endogenous melusin gene, wherein said mouse lacks expression of endogenous melusin, and wherein said mouse, after being subjected to a hypertensive condition, develops at least a phenotype selected from the group consisting of impaired heart hypertrophy, heart dilation, and heart failure, said method comprising:

a) disrupting by homologous recombination the gene encoding melusin in a mouse embryonic stem (ES) cell,

(b) injecting said ES cell into a mouse blastocyst,

(c) implanting said blastocyst into the uterus of a foster mother mouse to generate a chimeric embryo,

(d) obtaining a chimeric mouse which has germ line cells comprising a disrupted gene encoding melusin from said chimeric embryo,

(e) breeding said chimeric mouse with a different mouse strain, and

(f) selecting a male transgenic mouse comprising a disruption of the gene encoding melusin,

3) a method of producing a transgenic mouse comprising a disruption in its endogenous melusin gene, wherein said mouse lacks expression of endogenous melusin, further comprising breeding a male transgenic mouse comprising a disruption in its endogenous melusin gene with a female transgenic mouse comprising a heterozygous or homozygous disruption in its endogenous melusin gene, and selecting a homozygous female mouse comprising disrupted genes encoding melusin,

4) a method of selecting a compound that is pharmacologically active in the treatment of heart failure, said method comprising:

i) inducing a hypertensive condition in the transgenic mouse comprising a disruption in its endogenous melusin gene, wherein said mouse lacks expression of endogenous melusin, and wherein said mouse, after being subjected to a hypertensive condition, develops at least a phenotype selected from the group consisting of impaired heart hypertrophy, heart dilation, and heart failure,

ii) administering compounds to said mouse,

iii) selecting a compound that is pharmacologically active in the treatment of heart failure.

5) A method of selecting a compound that is pharmacologically active in the treatment of heart failure, said method comprising:

i) inducing a hypertensive condition in the cells obtained from a mouse comprising a disruption in its endogenous melusin gene, wherein said mouse lacks expression of endogenous melusin, and wherein said mouse, after being subjected to a

hypertensive condition, develops at least a phenotype selected from the group consisting of impaired heart hypertrophy, heart dilation, and heart failure,

i) administering compounds to the said cells,

iii) selecting a compound that is pharmacologically active in the treatment of heart failure,

6) A method of selecting a compound that is pharmacologically active in the prevention of heart failure, said method comprising:

i) administering compounds to the transgenic mouse comprising a disruption in its endogenous melusin gene, wherein said mouse lacks expression of endogenous melusin, and wherein said mouse, after being subjected to a hypertensive condition, develops at least a phenotype selected from the group consisting of impaired heart hypertrophy, heart dilation, and heart failure,

ii) inducing a hypertensive condition in said mouse,

iii) selecting a compound that is pharmacologically active in the prevention of heart failure

7) A method of selecting a compound that is pharmacologically active in the prevention of heart failure, said method comprising:

i) administering compounds to the cells obtained from a mouse comprising a disruption in its endogenous melusin gene, wherein said mouse lacks expression of endogenous melusin, and wherein said mouse, after being subjected to a hypertensive condition, develops at least a phenotype selected from the group consisting of impaired heart hypertrophy, heart dilation, and heart failure,

ii) inducing a hypertensive condition in said cells,

iii) selecting a compound that is pharmacologically active in the prevention of heart failure.

does not reasonably provide enablement for:

1) a transgenic mouse comprising a disruption of the gene or genes encoding melusin, wherein said mouse, after being subjected to a hypertensive condition, develops at least a phenotype selected from the group consisting of impaired heart hypertrophy, heart dilation, and heart failure and

2) a transgenic mouse comprising a heterozygous disruption of the gene encoding melusin, wherein said mouse, after being subjected to a hypertensive condition, develops at least a phenotype selected from the group consisting of impaired heart hypertrophy, heart dilation, and heart failure,

3) a method of producing a transgenic mouse comprising disruption of the gene encodinq melusin, wherein said disruption inhibits expression of wild type melusin, said method :

a) disrupting by homologous recombination the gene encoding melusin in a mouse embryonic stem (ES) cell,

(b) injecting said ES cell into a mouse blastocyst,

(c) implanting said blastocyst into the uterus of a foster mother mouse to generate a chimeric embryo,

(d) obtaining a chimeric mouse which has germ line cells comprising a disrupted gene encoding melusin from said chimeric embryo,

(e) breeding said chimeric mouse with a different mouse strain, and

(f) selecting a transgenic mouse comprising a disruption of the gene encoding melusin.

4) a method of screening compounds for pharmacological activity, said method comprising:

i) administering compounds to the transgenic mouse comprising a disruption of the gene or genes encoding melusin, wherein said mouse, after being subjected to a hypertensive condition, develops at least a phenotype selected from the group consisting of impaired heart hypertrophy, heart dilation, and heart failure,

ii) selecting a compound that is pharacologically active in the prevention and/or treatment of heart failure.

5) a method of screening compounds for pharmacological activity, said method comprising:

i) administering compounds to the cells obtained from the transgenic mouse comprising a disruption of the gene or genes encoding melusin, wherein said mouse, after being subjected to a hypertensive condition, develops at least a phenotype selected from the group consisting of impaired heart hypertrophy, heart dilation, and heart failure,

ii) selecting a compound that is pharacologically active in the prevention and/or treatment of heart failure.

6) a method of studying a heart pathology, said method comprising:

i) exposing the transgenic mouse comprising a disruption of the gene or genes encoding melusin, wherein said mouse, after being subjected to a hypertensive condition, develops at least a phenotype selected from the group consisting of impaired heart hypertrophy, heart dilation, and heart failure to hypertensive conditions and

ii) studying the development of a heart pathology in said mouse, wherein said pathology is selected from the group consistinf of heart failure, congestive heart failure, dialated cardiomyopathy, hypertensive cardiomyopathy, hypertrophic cardiomyopathy, and heart infarct.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's amendments raise new issues of enablement. Response to Applicant's rebuttals of April 7, 2008 follows the new issues of enablement.

Claim 1 has been amended and encompasses heterozygous female mice that express wild type melusin and exhibit no phenotype. Nothing in the art or the specification teaches that heterozygous mice comprising a disruption in melusin exhibits the phenotypes as listed in claim 1. Further, as far as can be told, the heterozygous female mice are not disclosed as exhibiting any phenotype. Subsequently, neither the specification nor the art provides any guidance for using a mouse with no phenotype. Similarly, while claim 24 indicates that the claimed method makes mice that express no wild type melusin, it is noted that the method does not indicate how to exclude female

heterozygous mice that express wild type melusin such that the method can be practiced.

Applicant's arguments, see page 6 of Applicant's response, filed April 7, 2008, with respect to the rejection of claims 1-25, 40-42 have been fully considered and are persuasive. As such, the rejection as they apply to the Office Action of January 7, 2008 is withdrawn. However, Applicant's amendments raise new issues of rejection, as discussed above. To reiterate, the claims encompass heterozygous female mice and nothing in the art or specification indicates that heterozygous females exhibit any of the phenotypes listed in claim 1. Further, nothing in the art or specification teaches how to use mice that exhibit no phenotype.

As such, the claims remain rejected.

It is noted that the rejection of claims 2-7, 16, 21, 22, 40-42 is withdrawn as the claims are cancelled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 17 is newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 17 depends on claim 16, a cancelled claim. In the interest of compact prosecution, claim 17 has been interpreted to depend on claim 1.

Claims 18, 23 are newly rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is that the mice or cells need to be induced with a hypertensive condition such that the compounds can be screened to see the effect of the compound. In addition to this issue, in the method of screening for compounds that treatment of heart failure, an artisan would need to induce the hypertensive condition, administer the compound, and then select a compound. In the method of screening for compounds that prevent heart failure, an artisan would need to administer the compound, induce the hypertensive condition, and then select a compound.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Mondays, Tuesdays, Thursdays, and Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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